

LISTING OF CLAIMS

81
1. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,
and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2,
and a H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 comprise murine
monoclonal CC49 antibody Complementarity Determining Regions (CDRs) and at least one of
L-CDR1 and L-CDR2 ~~comprises~~ are a human monoclonal LEN antibody Complementarity
Determining Region (CDR) ~~L-CDR1 and L-CDR2,~~

wherein the humanized CC49 antibody retains binding affinity for TAG-
72 and has reduced immunogenicity, as compared to a parental humanized CC49 antibody.

2. (Currently amended) The humanized antibody of claim 1, wherein L-CDR1
~~comprises~~ is the human monoclonal LEN antibody ~~CDR~~ L-CDR1.

3. (Canceled)

4. (Currently amended) The humanized antibody of claim 1, wherein L-CDR2
~~comprises~~ is the human monoclonal LEN antibody ~~CDR~~ L-CDR2.

5. (Canceled)

6. (Currently amended) The humanized antibody of claim 1, wherein both L-CDR1
and L-CDR2 ~~comprise~~ are human monoclonal LEN antibody ~~CDRs~~ L-CDR1 and L-CDR2,
respectively.

7-9. (Canceled)

10. (Currently amended) The humanized antibody of claim 1, wherein the parental
humanized CC49 antibody comprises three ~~light chain hypervariable regions~~ L-CDRS and three

~~heavy chain hypervariable regions~~ H-CDRs of the murine monoclonal CC49 antibody, a variable light chain framework of a human monoclonal LEN antibody, and a variable heavy chain framework of a human monoclonal 21/28'CL antibody.

11. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,
and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2,
and a H-CDR3,

wherein at least L-CDR3, H-CDR1, H-CDR2 and H-CDR3 ~~comprise~~ are
murine CC49 monoclonal antibody ~~Complementarity Determining Regions (CDRs)~~ L-CDR3, H-
CDR1, H-CDR2 and H-CDR3, and wherein L-CDR1 and L-CDR2 are murine CC49 antibody or
human LEN antibody L-CDR1 and L-CDR2, and wherein at least one amino acid at position-60,
61, 62, or 64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding
position in the human monoclonal 21/28'CL antibody,

wherein the humanized CC49 antibody retains binding affinity for TAG-
72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

12. (Previously presented) The humanized antibody of claim 11, wherein an
asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

13. (Previously presented) The humanized antibody of claim 11, wherein a threonine
at position 97 of the murine CC49 L-CDR3 is replaced with a serine.

14. (Canceled)

15. (Currently amended) The humanized antibody of claim 11, wherein L-CDR1
~~comprises~~ is a human monoclonal LEN antibody ~~Complementarity Determining Region~~
~~(CDR)~~ L-CDR1.

16. (Canceled)

17. (Currently amended) The humanized antibody of claim 11, wherein L-CDR2 ~~comprises~~ is a human monoclonal LEN antibody CDR1-CDR2.

18. (Canceled)

19. (Currently amended) The humanized antibody of claim 11, wherein both L-CDR1 and L-CDR2 ~~comprise~~ are human monoclonal LEN antibody Complementarity Determining Regions L-CDR1 and L-CDR2, respectively.

20. (Canceled)

21. (Previously presented) The humanized antibody of claim 11, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

22. (Previously presented) The humanized antibody of claim 11, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

23. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2, and a H-CDR3,

wherein at least L-CDR3, H-CDR1, H-CDR2 and H-CDR3 ~~comprise~~ are murine CC49 monoclonal antibody L-CDR3, H-CDR1, H-CDR2 and H-CDR3, and wherein L-CDR1 and L-CDR2 are murine CC49 antibody or human LEN antibody L-CDR1 and L-CDR2, Complementarity Determining Regions (CDRs), and wherein a threonine at position 97 in the murine CC49 L-CDR3 is replaced with a serine,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

24. (Previously presented) The humanized antibody of claim 23, wherein at least one amino acid of positions 60, 61, 62, or 64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding position in the human monoclonal 21/28'CL antibody.

25. (Canceled)

26. (Currently amended) The humanized antibody of claim 23, wherein L-CDR1 ~~comprises is~~ is a human monoclonal LEN antibody Complementarity Determining Region (CDR)L-CDR1.

27. (Canceled)

28. (Currently amended) The humanized antibody of claim 23, wherein L-CDR2 ~~comprises is~~ is a human monoclonal LEN antibody CDRL-CDR2.

29. (Canceled)

30. (Currently amended) The humanized antibody of claim 23, wherein both L-CDR1 and L-CDR2 ~~comprise are~~ are human monoclonal LEN antibody Complementarity Determining RegionsL-CDR1 and L-CDR2, respectively.

31-33. (Canceled)

34. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining (H-CDR)1, a H-CDR2, and a H-CDR3,
wherein L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 antibody, and

wherein (1) a threonine is at position 94 in the L-CDR3, or (2) a serine is at position 97 in the L-CDR3, or (3) a threonine is at position 94 and a serine is at position 97 in the L-CDR3,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

35. (Previously presented) The humanized antibody of claim 34, wherein the threonine is at position 94 in the L-CDR3.

36-37. (Canceled)

38. (Previously presented) A pharmaceutical composition, comprising a therapeutically effective amount of the humanized antibody of claim 1 in a pharmaceutically acceptable carrier.

39. (Canceled)

40. (Previously presented) A composition comprising a functional fragment of the humanized antibody of claim 1, wherein the functional fragment specifically binds TAG-72.

41. (Previously presented) The composition of claim 40, wherein the fragment comprises an Fv, an Fab, or an F(ab')₂.

42-47. (Canceled)

48. (Previously presented) The humanized antibody of claim 2, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

49. (Previously presented) The humanized antibody of claim 4, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

50. (Previously presented) The humanized antibody of claim 6, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

51. (Previously presented) The humanized antibody of claim 11, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

52. (Previously presented) The humanized antibody of claim 11, wherein the amino acid at the corresponding position in the human monoclonal 21/28'CL antibody comprises an amino acid corresponding to position 12, 13, 14, or 16 of the amino acid sequence as set forth in SEQ ID NO: 11.

53. (Currently amended) The humanized antibody of claim 11, wherein the parental humanized CC49 antibody comprises three ~~light chain hypervariable regions~~L-CDRs and three ~~heavy chain hypervariable regions~~H-CDRs from the murine monoclonal CC49 antibody, a variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

54. (Previously presented) The humanized antibody of claim 15, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

55. (Previously presented) The humanized antibody of claim 17, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

56. (Previously presented) The humanized antibody of claim 19, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

57. (Currently amended) The humanized antibody of claim 23, wherein the parental humanized CC49 antibody comprises three ~~light chain hypervariable regions~~L-CDRs and three ~~heavy chain hypervariable regions~~H-CDRs from the murine monoclonal CC49 antibody, a

variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

58. (Previously presented) The humanized antibody of claim 24, wherein the amino acid at the corresponding position in the human monoclonal 21/28'CL antibody comprises amino acid 12, 13, 14, or 16, respectively, of an amino acid sequence as set forth in SEQ ID NO: 11.

59. (Previously presented) The humanized antibody of claim 24, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

60. (Previously presented) The humanized antibody of claim 24, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

21 61. (Previously presented) The humanized antibody of claim 24, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

62. (Previously presented) The humanized antibody of claim 24, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

63. (Previously presented) The humanized antibody of claim 26, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

64. (Previously presented) The humanized antibody of claim 28, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

65. (Previously presented) The humanized antibody of claim 30, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

66. (Previously presented) The humanized antibody of claim 34, wherein the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

67. (Previously presented) The humanized antibody of claim 34, wherein the threonine is at position 94 in the L-CDR3 from the murine CC49 antibody and the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

68. (Previously presented) The humanized antibody of claim 11, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine, a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine, an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine, and a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

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Amend.
69. (Currently amended) A kit comprising a container comprising the humanized antibody of claim 1 and instructions for using the humanized antibody to treat or detect a cancer cell expressing TAG-72.
